REMARKS

Claims 1-5, 29-36, 38-52 and 54-59 are pending in the above-identified application. Of the pending claims, Claims 58 and 59 are allowed. Claims 1-5, 29-36, 38-52 and 55-57 are rejected under 35 U.S.C. §102, as discussed below. Claim 1 is amended to recite a composition comprising a sufficient number of a first isolated T cell to be suitable as an adoptive immunotherapeutic. Claim 42 is amended to recite a composition comprising at least a first and a second isolated T cell population, wherein said first population comprises a sufficient number of a first T cell to be suitable as an adoptive immunotherapeutic for an animal, and wherein said second population comprises a sufficient number of a second T cell to be suitable as an adoptive immunotherapeutic for an animal. Support for these amendments can be found, for example, on page 107, line 21 to page 108, line 16 of the specification as filed. Claims 38 and 39 are cancelled without prejudice or disclaimer. No new matter is added by any of these amendments. Upon entry of the amendments, claims 1-5, 29-36, 40-52 and 54-59 are presented for further examination.

Rejection of Claims Under 35 U.S.C. §102

Claims 1-5, 29-36, 38-52 and 55-57 are rejected under 35 U.S.C. §102(b) as allegedly being anticipated by Zajac *et al.* (1997. *Int J Cancer* 71:491-496, hereinafter referred to as "Zajac"), Kittlesen *et al.* (1998. *J Immunol* 160:2099-2106, hereinafter referred to as "Kittlesen"), or Jager *et al.* (1998. *J Exp Med* 187:265-270, hereinafter referred to as "Jager"). Applicants respectfully disagree that cited references anticipate the pending claims as discussed below.

The Law of Anticipation

Anticipation under Section 102 can be found only if a reference shows exactly what is claimed. *Titanium Metals Corp. v. Banner*, 778 F.2d 775 (Fed. Cir. 1985). More particularly, a finding of anticipation requires the disclosure in a single piece of prior art of **each and every** limitation of a claimed invention. *Electro Med. Sys. S.A. v. Cooper Life Sciences*, 34 F.3d 1048, 1052 (Fed. Cir. 1994). "To anticipate, every element and limitation of the claimed invention must be found in a single prior art reference, arranged as in the claim." *Brown v. 3M*, 265 F.3d 1349 (Fed. Cir. 2001).

The Claims

The amended claims relate to compositions that comprise a sufficient number of a T cell to be suitable as an adoptive immunotherapeutic. In some embodiments, the claimed compositions contain an isolated T cell expressing a T cell receptor specific for an MHC-peptide complex containing a housekeeping epitope. In other embodiments, the claimed compositions contain at least a first and a second isolated T cell population, wherein the first and second T cell populations recognize two different housekeeping epitopes. Accordingly, amended Claim 1 recites a composition comprising a sufficient number of a first isolated T cell to be suitable as an adoptive immunotherapeutic. Claims 2-5, 29-36 and 40-41 depend from independent Claim 1 and thus contain all the features thereof as well as additional features recited within the claims. Claims 38 and 39 are cancelled without prejudice or disclaimer. Amended Claim 42 recites a composition comprising at least a first and a second isolated T cell population, wherein said first population comprises a sufficient number of a first T cell to be suitable as an adoptive immunotherapeutic for an animal, and wherein said second population comprises a sufficient number of a second T cell to be suitable as an adoptive immunotherapeutic for an animal. Claims 43-52 and 55-57 depend from independent Claim 42 and thus contain all the features thereof as well as additional features recited within the claims.

Zajac Does Not Anticipate the Claims

The rejection of claims 1-5, 29, 30, 33-35, 38-52 and 55-57 was maintained under 35 U.S.C. §102(b) as allegedly being anticipated by Zajac *et al.* (1997. *Int J Cancer* 71:491-496, hereinafter referred to as "Zajac"). The Examiner asserted that there is no limitation in the claims regarding any type of therapeutic effect attributable to the administered cells, and that all that is required is that the cells can be taken up in some manner and administered to a human subject, which is not prevented by the low cell number in the sample taught by Zajac.

Zajac discloses generation of tumoricidal lymphocytes from healthy donors after *in vitro* stimulation with a replication-incompetent *Vaccinia* virus encoding MART-1/Melan-A 27-35 epitope. However, Zajac does not teach compositions that are suitable as an adoptive immunotherapeutic. The Examiner has previously acknowledged that the T cells ultimately derived and disclosed by Zajac are not suitable for adoptive administration to a human because, during generation of MART-1/Melan-A_{27-35}-specific CTLs, the T cells are exposed to agents

which render the compositions unsuitable for adoptive administration to a human. For example, the compositions used in generating MART-1/Melan-A_{27-35}-specific CTLs by Zajac contain antibiotics and 10 units/ml recombinant human IL-2, which render these compositions unsuitable for administration to a human. For at least the same reasons, the disclosed compositions are also not suitable for adoptive administration to an animal. Moreover, the initial T cell populations disclosed in Zajac do not exhibit any detectable reactivity against the MART-1/Melan-A_{27-35} peptide. Thus, Zajac does not teach that TILs obtained from a melanoma patient include any number, let alone a sufficient number, of a first T cell to be suitable as an adoptive immunotherapeutic. Zajac therefore does not teach each and every feature of the claims.

Accordingly, Applicants respectfully submit that the reference does not anticipate the claims. Withdrawal of the rejection is requested.

Kittlesen Does Not Anticipate the Claims

The rejection of claims 1-5, 29, 30, 33, 34, 36 and 38-41 was maintained under 35 U.S.C. §102(b) as allegedly being anticipated by Kittlesen *et al.* (1998. *J Immunol* 160:2099-2106, hereinafter referred to as "Kittlesen"). The Examiner argued that there is no limitation in the claims regarding any type of therapeutic effect attributable to the administered cells, and that all that is required is that the cells can be taken up in some manner and administered to a human subject, which is not prevented by the low cell number in the sample taught by Kittlesen.

Kittlesen teaches recognition by human melanoma patients of an HLA-A1-restricted epitope from tyrosinase containing two cysteine residues. However, Kittlesen discloses that CTLs derived from peripheral blood lymphocytes, tumor-involved nodes, or tumor-draining nodes are cultured *in vitro* and repeatedly stimulated with autologous tumor cells. The cells are cultured in medium with fetal calf serum, glutamine and antibiotics, and the presence of such components in the medium renders the disclosed compositions unsuitable for adoptive administration to a human and therefore unsuitable as an adoptive immunotherapeutic. Moreover, no tyrosinase-reactivity is reported for T cells directly obtained from a melanoma patient. Thus, the disclosed compositions do not include a sufficient number of a first T cell to be suitable as an adoptive immunotherapeutic. Kittlesen therefore does not teach and every feature of the claims.

Accordingly, Applicants respectfully submit that the reference does not anticipate the claims. Withdrawal of the rejection is requested.

Jager Does Not Anticipate the Claims

The rejection of claims 1-5, 29-32, 35 and 38-41 was maintained under 35 U.S.C. §102(b) as allegedly being anticipated by Jager *et al.* (1998. *J Exp Med* 187:265-270, hereinafter referred to as "Jager"). The Examiner argued that there is no limitation in the claims regarding any type of therapeutic effect attributable to the administered cells, and that all that is required is that the cells can be taken up in some manner and administered to a human subject, which is not prevented by the low cell number in the sample taught by Jager.

Jager teaches the antigen-specific humoral and cellular immune responses against human tumor antigens. However, to obtain the stable CTL line NW38-IVS-1, Jager cultured mixed lymphocyte tumor cell cultures of peripheral blood lymphocytes (PBLs) and the autologous tumor cell line from patient NW38 in medium containing antibiotics. The presence of antibiotics in the medium used to culture CTLs renders the CTL composition unsuitable for adoptive administration to a human and therefore unsuitable as an adoptive immunotherapeutic. Furthermore, Jager discloses that the needle biopsy obtained from a melanoma patient was used to establish the tumor cell line NW-MEL-38; such cells are clearly tumor cells, not reactive T cells. Jager only discloses NY-ESO-1 reactive T cells after mixed lymphocyte tumor cell cultures of PBLs and NW-MEL-38. Thus, Jager does not teach that PBLs obtained from a melanoma patient include any number, let alone a sufficient number, of a first T cell to be suitable as adoptive immunotherapeutic. Jager therefore does not teach each and every feature of the claims.

Accordingly, Applicants respectfully submit that the reference does not anticipate the claims. Withdrawal of the rejection is requested.

Objection-to Claim 54 and Allowable Subject Matter: Allowed Claims 58 and 59

The Examiner objected to Claim 54 as being dependent upon a rejected base claim, but stated that Claim 54 would be allowable if rewritten in independent form to include all of the limitations of the base claim and any intervening claims.

Claim 54 was previously amended to include all the limitations of base Claim 42. Accordingly, Applicants respectfully request that the objection to Claim 54 be withdrawn.

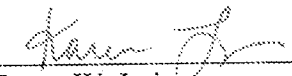
Claims 58 and 59 are allowed.

Conclusion

Applicants submit that the present Application is in condition for allowance and respectfully request the same. If any issues remain with respect to the restriction requirement, the Examiner is cordially invited to contact Applicants' representative at the number provided below in order to resolve such issues promptly.

Please charge any additional fees, including any fees for additional extension of time, or credit overpayment to Deposit Account No. 19-3140.

Respectfully submitted,

Dated: February 28, 2008 By: 

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